

CLAIMS

1. A therapeutic agent for cibophobia comprising, as an active ingredient, a substance that suppresses expression or
5 function of a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO:4.
2. A therapeutic agent for cibophobia comprising, as an active ingredient, a nucleic acid of the following (a) or (b):
10 (a) a nucleic acid consisting of a base sequence complementary to a base sequence shown in SEQ ID NO: 1 or SEQ ID NO: 3
(b) a nucleic acid consisting of a base sequence capable of hybridizing with a nucleic acid consisting of a base sequence shown in SEQ ID NO: 1 or SEQ ID NO: 3 or a primary transcript
15 which generates said base sequence after post-transcriptional processing under physiological conditions of hypothalamus of a subject animal for treatment, and which is capable of inhibiting translation into a polypeptide encoded by the base sequence shown in SEQ ID NO:
20 1 or SEQ ID NO: 3 under a hybridized state.
3. A therapeutic agent for cibophobia comprising, as an active ingredient, a substance which shows a specific affinity for a polypeptide consisting of an amino acid sequence shown in
25 SEQ ID NO: 2 or SEQ ID NO: 4 and which inhibits a functional expression of said polypeptide.
4. The therapeutic agent for cibophobia of claim 3, wherein the substance is a nucleic acid.
- 30 5. The therapeutic agent for cibophobia of claim 3, wherein the substance is an antibody.

6. A therapeutic agent for cibophobia comprising, as an active ingredient, an expression vector encoding the nucleic acid of claim 2 or 4.
- 5 7. A therapeutic agent for cibophobia comprising, as an active ingredient, a host cell transfected with the expression vector of claim 6.
8. A therapeutic agent for a lifestyle-related disease
10 comprising, as an active ingredient, a substance that enhances expression or function of a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4.
- 15 9. A therapeutic agent for a lifestyle-related disease comprising, as an active ingredient, a polypeptide of any of the following (a) to (c):
(a) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO:4
20 (b) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO:4, wherein one or more amino acids of the amino acid sequence have been substituted, deleted, inserted, added or modified, which shows a ligand - receptor interaction of the same level as the polypeptide
25 of (a), and which is coupled with a G protein α subunit and shows an activity to promote a GDP/GTP exchange reaction of the subunit
(c) a polypeptide which is an ortholog of the polypeptide of (a).
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10. A therapeutic agent for a lifestyle-related disease comprising, as an active ingredient, an expression vector comprising a nucleic acid encoding the polypeptide of claim

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11. A therapeutic agent for a lifestyle-related disease comprising, as an active ingredient, a host cell transfected
5 with the expression vector of claim 10.

12. The therapeutic agent for a lifestyle-related disease of any of claims 8 to 11, which is a feeding suppressant, an anti-obesity agent, an anti-diabetic agent or an
10 anti-hyperlipidemic agent.

13. A screening system for a substance having a therapeutic activity against cibophobia or a lifestyle-related disease, which comprises, as one constitution unit, a system
15 comprising, as constituent elements, a lipid bilayer membrane comprising a polypeptide of any of the following (a) to (c):

(a) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4

20 (b) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4, wherein one or more amino acids of the amino acid sequence have been substituted, deleted, inserted, added or modified, which shows a ligand - receptor interaction of the same level as the polypeptide
25 of (a), and which is coupled with a G protein α subunit and shows an activity to promote a GDP/GTP exchange reaction of the subunit,

(c) a polypeptide which is an ortholog of the polypeptide of (a), and a polypeptide comprising at least a
30 receptor-binding region of a G protein α subunit belonging to a certain family and a guanine nucleotide-binding region of any G protein α subunit, wherein said constitution unit is present in a receptor-binding regions of each family of

the G protein α subunit.

14. The screening system of claim 13, wherein the constitution unit comprises an eucaryotic host cell transfected with an expression vector comprising a DNA encoding the polypeptide of any of (a) to (c), and an expression vector comprising a DNA encoding a polypeptide comprising at least a receptor-binding region of a G protein α subunit belonging to a certain family and a guanine nucleotide-binding region of any G protein α subunit, a homogenate of said cell or a membrane fraction derived from said cell.

15. The screening system of claim 13, wherein the constitution unit comprises an eucaryotic host cell transfected with an expression vector comprising a DNA encoding a polypeptide fused with a polypeptide comprising, on a C terminal of the polypeptide of any of (a) to (c), at least a receptor-binding region of a G protein α subunit belonging to a certain family and a guanine nucleotide-binding region of any G protein α subunit, a homogenate of said cell or a membrane fraction derived from said cell.

16. The screening system of any of claims 13 to 15, wherein the polypeptide in each constitution unit, which comprises a receptor-binding region of a G protein α subunit and a guanine nucleotide-binding region of any G protein α subunit, further comprises the same effector interacting region and the lipid bilayer membrane further comprises an effector that interacts with said region.

17. The screening system of any of claims 13 to 16, wherein the therapeutic activity against lifestyle-related diseases is a feeding suppressive activity, an anti-obesity activity,

an anti-diabetic activity or an anti-hyperlipidemic activity.

18. A screening method for a substance having a therapeutic
5 activity against cibophobia or a lifestyle-related disease,
which comprises adding, in each constitution unit of the
screening system of any of claims 13 to 15, a labeled GTP
analog in the presence and absence of a test substance and
comparing an amount of the label bound with a guanine
10 nucleotide-binding region under the both conditions.

19. A screening method for a substance having a therapeutic
activity against cibophobia or a lifestyle-related disease,
which comprises comparing, in each constitution unit of the
15 screening system of claim 16, an activity of the effector
in the presence and absence of the test substance.

20. A method for identifying a G protein α subunit capable
of coupling with a polypeptide consisting of an amino acid
20 sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4, which comprises
adding, in each constitution unit of the screening system
of any of claims 13 to 15, a labeled GTP analog in the presence
and absence of a ligand for said polypeptide, and comparing
an amount of the label bound with a guanine nucleotide-binding
25 region among constitution units.

21. A method for identifying a G protein α subunit capable
of coupling with a polypeptide consisting of an amino acid
sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4, which comprises
30 comparing, in each constitution unit of the screening system
of claim 16, an activity of the effector in the presence and
absence of a ligand for said polypeptide.

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22. A screening method for a substance having a therapeutic activity against cibophobia or a lifestyle-related disease, which comprises applying the method of claim 18 or 19 only to a system comprising, as a constituent element, a
5 polypeptide comprising a receptor-binding region of the G protein α subunit as identified by the method of claim 20 or 21.

23. The method of claim 22, wherein the G protein α subunit
10 belongs to a Gs family.

24. A screening system for a ligand for a polypeptide of any of the following (a) to (c):

(a) a polypeptide consisting of an amino acid sequence shown
15 in SEQ ID NO: 2 or SEQ ID NO: 4

(b) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4, wherein one or more amino acids of the amino acid sequence have been substituted, deleted, inserted, added or modified, which shows a ligand
20 - receptor interaction of the same level as the polypeptide of (a), and which is coupled with a G protein α subunit belonging to a Gs family and shows an activity to promote a GDP/GTP exchange reaction of the subunit,

(c) a polypeptide which is an ortholog of the polypeptide
25 of (a), which comprises, as constituent elements, a lipid bilayer membrane comprising said polypeptide and a polypeptide comprising at least a receptor-binding region of a G protein α subunit belonging to a Gs family and a guanine nucleotide-binding region of any G protein α subunit.

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25. The screening system of claim 24, which comprises an eucaryotic host cell transfected with an expression vector comprising a DNA encoding the polypeptide of any of (a) to

(c), and an expression vector comprising a DNA encoding a polypeptide comprising at least a receptor-binding region of a G protein α subunit belonging to a Gs family and a guanine nucleotide-binding region of any G protein α subunit, a
5 homogenate of said cell or a membrane fraction derived from said cell.

26. The screening system of claim 24, which comprises an eucaryotic host cell transfected with an expression vector
10 comprising a DNA encoding a polypeptide fused with a polypeptide comprising, on a C terminal side of said polypeptide, any of (a) to (c), at least a receptor-binding region of a G protein α subunit belonging to a Gs family and a guanine nucleotide-binding region of any G protein α subunit,
15 a homogenate of said cell or a membrane fraction derived from said cell.

27. The screening system of any of claims 24 to 26, wherein the polypeptide comprising a receptor-binding region of a
20 G protein α subunit belonging to a Gs family and a guanine nucleotide-binding region of any G protein α subunit further comprises any effector interacting region and the lipid bilayer membrane further comprises an effector that interacts with said region.

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28. The screening system of claim 27, wherein the effector is adenylate cyclase.

29. The screening system of any of claims 24 to 28, which
30 is a system for searching a substance having a therapeutic activity against cibophobia or a lifestyle-related disease.

30. The screening system of claim 29, wherein the therapeutic

activity against a lifestyle-related disease is a feeding suppressive activity, an anti-obesity activity, an anti-diabetic activity or an anti-hyperlipidemic activity.

5 31. A screening method for a ligand for a polypeptide of any of the following (a) to (c):

(a) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4

(b) a polypeptide consisting of an amino acid sequence shown
10 in SEQ ID NO: 2 or SEQ ID NO: 4, wherein one or more amino acids of the amino acid sequence have been substituted, deleted, inserted, added or modified, which shows a ligand - receptor interaction of the same level as the polypeptide of (a), and which is coupled with a G protein α subunit
15 belonging to a Gs family and shows an activity to promote a GDP/GTP exchange reaction of the subunit,

(c) a polypeptide which is an ortholog of the polypeptide of (a),

which comprises adding, in the screening system of any
20 of claims 24 to 26 and in the presence and absence of a test substance, a labeled GTP analog, and comparing the amount of the label bound with a guanine nucleotide-binding region under the both conditions.

25 32. A screening method for a ligand for a polypeptide of any of the following (a) to (c):

(a) a polypeptide consisting of an amino acid sequence shown in SEQ ID NO: 2 or SEQ ID NO: 4

(b) a polypeptide consisting of an amino acid sequence shown
30 in SEQ ID NO: 2 or SEQ ID NO: 4, wherein one or more amino acids of the amino acid sequence have been substituted, deleted, inserted, added or modified, which shows a ligand - receptor interaction of the same level as the polypeptide

of (a), and which is coupled with a G protein α subunit belonging to a Gs family and shows an activity to promote a GDP/GTP exchange reaction of the subunit,
(c) a polypeptide which is an ortholog of the polypeptide
5 of (a),

which comprises comparing an activity of the effector in the screening system of claim 27 in the presence and absence of a test substance.

10 33. The screening method of claim 32, which comprises comparing an amount of cAMP in an eucaryotic host cell in the presence and absence of a test substance.

34. The screening method of any of claims 31 to 33, which
15 is a system for searching a substance having a therapeutic activity against cibophobia or a lifestyle-related disease.

35. The screening method of any of claims 18, 19, 22, 23 and 34, wherein the therapeutic activity against a
20 lifestyle-related disease is a feeding suppressive activity, an anti-obesity activity, an anti-diabetic activity or an anti-hyperlipidemic activity.

36. A therapeutic agent for cibophobia comprising, as an
25 active ingredient, a substance having a therapeutic activity against cibophobia, which is obtained by the screening method of any of claims 13-16, 18, 19, 22, 23, 29 and 34.

37. A therapeutic agent for a lifestyle-related disease
30 comprising, as an active ingredient, a substance having a therapeutic activity against a lifestyle-related disease, which is obtained by the screening method of any of claims 13-16, 18, 19, 22, 23, 29 and 34.